

66. (Amended) A method of claim 53, wherein the APP substrate comprises a human APP isoform and the determining step comprises measuring the production of amyloid alpha peptide (sAPP $\alpha$ ).

67. (Amended) A method of claim 53, wherein the method further comprises steps of:

(c) determining the level of hu-Asp1  $\alpha$ -secretase activity in the presence and absence of a modulator of hu-Asp1  $\alpha$ -secretase activity; and

(d) comparing the hu-Asp1  $\alpha$ -secretase activity in the presence and absence of the modulator, wherein modulators that increase hu-Asp1  $\alpha$ -secretase activity are identified as candidate Alzheimer's disease therapeutics.

68. (Amended) A method of claim 67, wherein the method further comprises a step of treating Alzheimer's Disease with said candidate Alzheimer's disease therapeutic.

70. (amended) The substrate of claim 69, wherein the substrate comprises a detectable label.